Concentration-dependent anti-inflammatory effects of dimethyl sulfoxide in macrophages in vitro

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INTRODUCTION

Dimethyl sulfoxide (DMSO) is a solvent widely used in biomedical research. It is known to interfere with cell signaling, but at a final concentration of 1% or lower is often deemed safe. One of the applications of DMSO is to dissolve hydrophobic compounds.

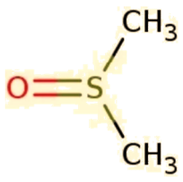

Figure 1. Dimethyl sulfoxide (DMSO) chemical structure.

During the characterization of a novel hydrophobic anti-inflammatory compound, we found that dilutions of 4 orders of magnitude of the compound diluted in DMSO, used at a 1% final concentration in cell culture media, strongly inhibited the lipopolysaccharide (LPS) induction of Interleukin (IL)-1b and Tumor Necrosis Factor (TNF)-a secretion without a dose-dependent effect ($p<0.001$ for all doses).

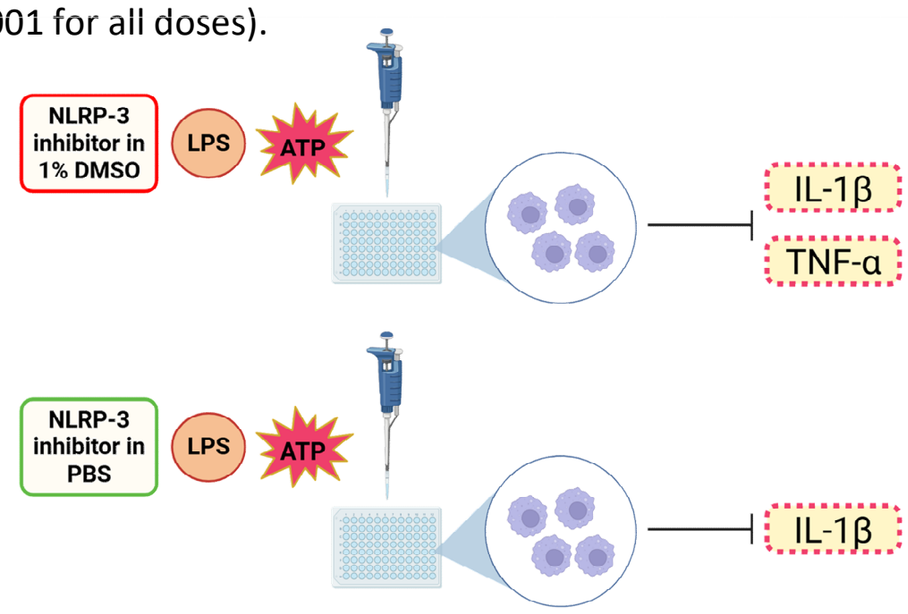

Figure 2. Experimental observation leading to hypothesis development.

Hypothesis: We hypothesized that DMSO could inhibit LPS-dependent cytokine release.

METHODS

We stimulated mouse macrophages (J774.1 cells) with LPS (1 µg/ml, 6h, to activate NF-kB-dependent gene expression) and administered ATP (5 mM, 30 min). LPS promotes TNF-a secretion and pro-IL-1b intracellular production, while ATP induces caspase-1-dependent IL-1b maturation and release. Cells were exposed to increasing concentrations of DMSO (0.2, 0.5, 1.0%). We collected the cell supernatants and performed ELISA assays to measure IL-1b and TNF-a production.

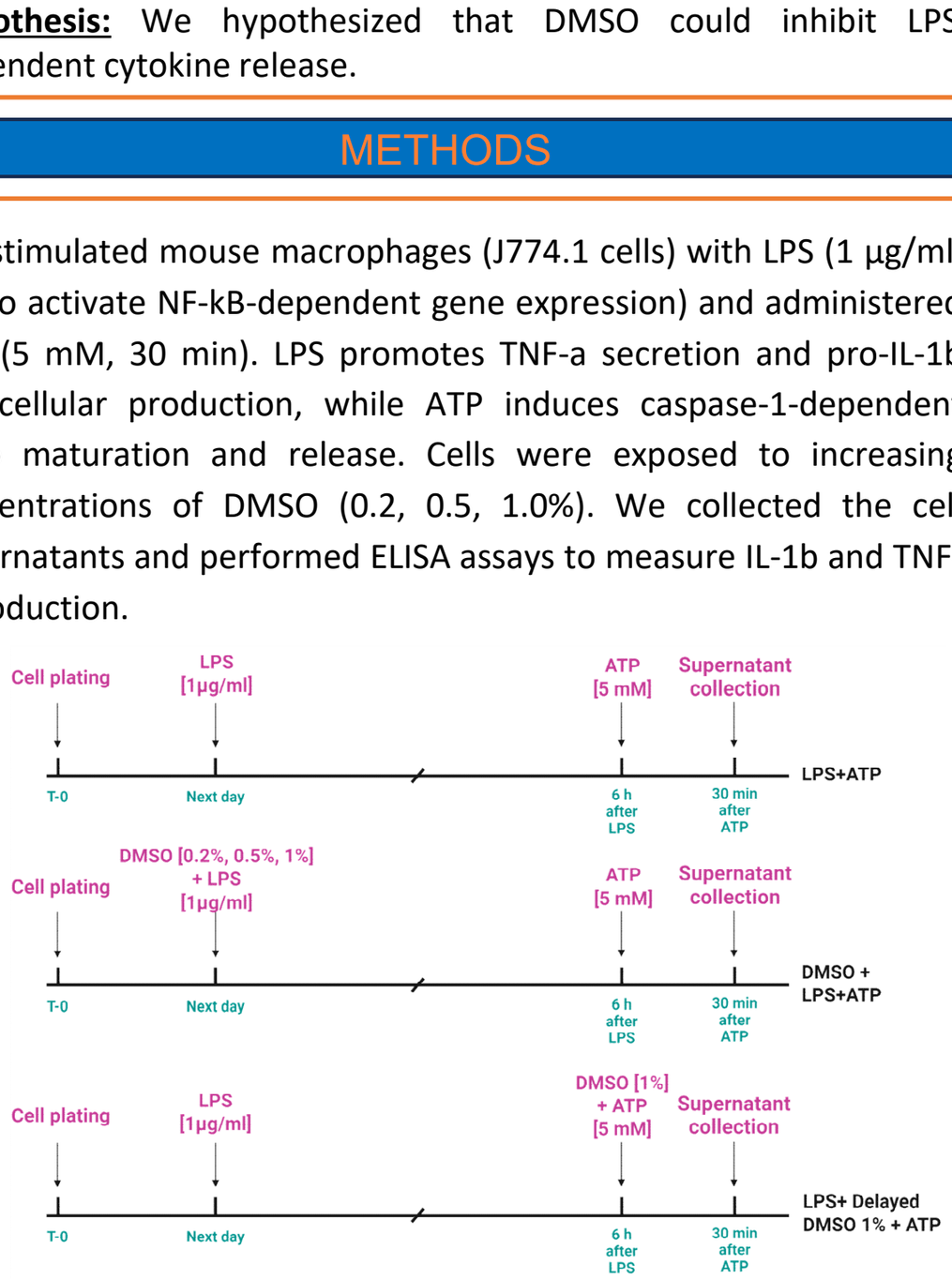

Figure 3. Experimental protocols.

RESULTS

The 1% dose of DMSO significantly reduced IL-1β secretion (205±12 vs 709±7 pg/ml; $p<0.0001$); 0.5% and 0.2% DMSO had no effect. DMSO at concentrations of 1.0% and 0.5% reduced TNF-α (1348±37 and 2672±25 vs 3125±27 pg/ml; all $p<0.0001$); 0.2% DMSO had no effect on TNF-α release.

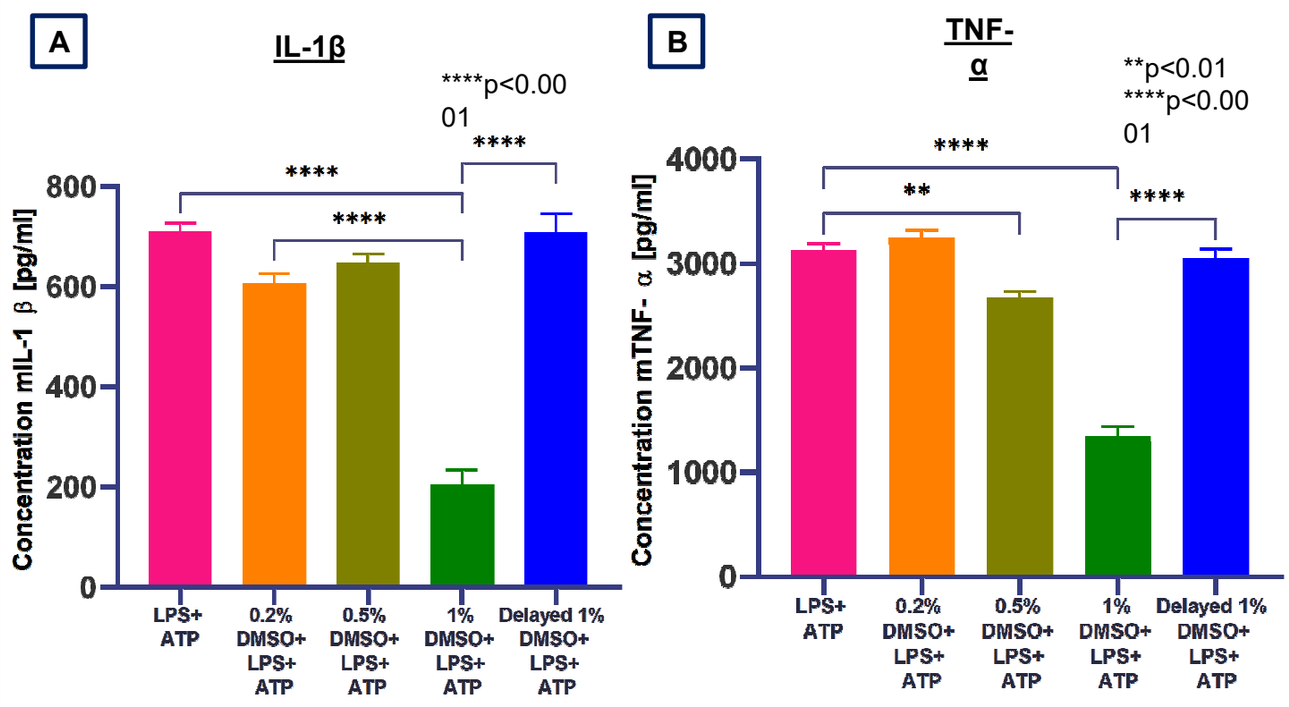

Figure 4. ELISA assay testing IL-1β and TNF-α concentration in vitro in mouse macrophages.

CONCLUSION

In conclusion, DMSO induces a dose-dependent inhibition of IL-1β and TNF-α by reducing LPS / NF-kB-dependent gene expression.

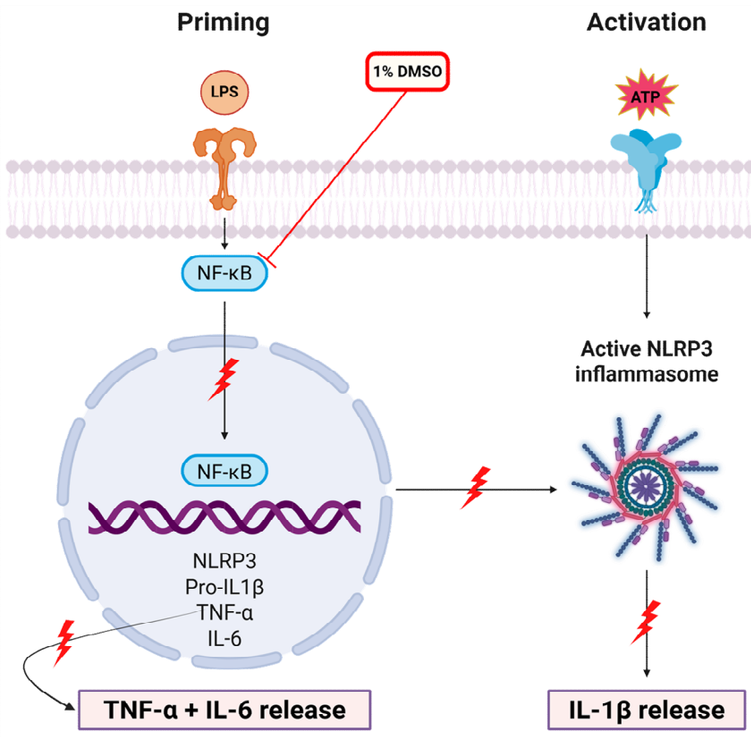

Figure 5. Summary of results and proposed mechanism.

Future prospective:

Further studies are warranted to elucidate the intracellular pathways involved and to determine how this solvent interacts with different drugs and cellular mechanisms.